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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/554,784	06/05/2000	MARK DE BOER	DEBOER2	1336

545 7590 04/22/2003

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EXAMINER	
DECLOUX, AMY M	

ART UNIT	PAPER NUMBER
1644	10

DATE MAILED: 04/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/554,784	DE BOER ET AL.	
	Examiner	Art Unit	
	Amy M. DeCloux	1644	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 11-22* is/are pending in the application.

4a) Of the above claim(s) *19-22* is/are withdrawn from consideration.

5)☒ Claim(s) *11,12 and 17* is/are allowed.

6)☒ Claim(s) *1-3,13-16 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 June 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's amendment filed 2-3-03, (Paper No. 19) is acknowledged and has been entered.

Claims 1-3 and 11-22 are pending.

Claims 19-22 have been withdrawn from consideration as not being drawn to the originally presented and examined product claims.

Claims 1-3 and 11-18 are under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

MAINTAINED Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 13 is not supported by the specification or by the claims as originally filed. There is no support in the specification or claims as originally filed for the recitation a composition comprising the monoclonal antibody of anyone of claims 1-3 "wherein the autoantigen is a heat shock protein that stimulates type 2 cytokine producing regulatory T-cells". There is no written description of the claimed invention in the specification or claims as originally filed. Thus the claimed invention constitutes **new matter.**

Response to Arguments

Applicant traverses this rejection on the grounds that pages 3-4 of the instant specification state that the present invention combines the administration of autoantigens with modulation of the cytokine microenvironment to enhance antigen therapy. The examiner notes that these said pages do not support the phrase "wherein the autoantigen is a heat shock protein that stimulates type 2 cytokine producing regulatory T-cells" because there is no mention of type 2 cytokines here.

Applicant further traverses the rejection on the grounds that page 5 of the instant specification discloses the combination of treatment with an autoantigen and an anti-IL12R beta-

2 chain antibody. Which is also encompassed by original claims 4 and 5. However, the examiner notes that these said pages do not support the phrase "wherein the autoantigen is a heat shock protein that stimulates type 2 cytokine producing regulatory T-cells" because there is no mention of type 2 cytokines here either.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

MAINTAINED Claims 1-3 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by EP0759466 A2.

'466 teaches antibodies and pharmaceutical compositions thereof that are capable of binding to cells expressing the IL-2 receptor proteins beta1 and beta2, and specifically teaches monoclonal antibodies to the human IL-12 beta2 receptor proteins and fragments thereof, which can be administered in clinical treatment of autoimmune diseases, wherein said antibodies block the binding of endogenous IL-12 to its receptor, (see entire patent, especially the Abstract and page 8, lines 9-12, 22-32). '466 also teaches that the high affinity IL-12 receptor is formed by the beta1 and beta2 chains which respond to IL-12 by causing cellular proliferation in a dose dependent manner, and that the beta2 protein contains cytoplasmic tyrosines likely used in signal transduction, (see entire article including examples 8-10). Therefore, the referenced teachings anticipate the claimed invention.

Response to Arguments

Applicant traverses the rejection on the grounds that the '466 application discloses antibodies which block the binding of IL-12 and doesn't teach the ability of these antibodies to block dimerization of the IL-12R beta 1 and beta 2 chains and prevent beta 2 chain mediated phosphorylation of STAT4. However the examiner notes that '466 teaches that the referenced antibodies block the binding of endogenous IL-12 to its receptor, and as such said antibodies would have the inherent properties of preventing beta 2 chain mediated phosphorylation of STAT4, because '466 also teaches that said properties are downstream events of binding by IL-12 to the high affinity IL-12 receptor. The examiner also notes that the referenced antibodies would have the inherent properties of blocking dimerization of the IL-12R beta 1 and beta 2 chains, because like the antibodies disclosed in the instant specification, said referenced antibodies are directed to the beta chain and as noted on page 7 of Applicant's response faxed 7-12-02, "one of skill would have recognized that the spectrum of antibodies which bind to IL12R beta-2 chain having functional characteristics claimed are implicitly disclosed as a result of the

isolation of the antigen". Accordingly, the referenced antibodies which bind to IL12R beta-2 chain have the inherent property of of blocking dimerization of the IL-12R beta 1 and beta 2 chains. Therefore the rejection is maintained, essentially for the reasons of record.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

MAINTAINED Claims 1-3, 14, 15 and 18 rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 759 466 in view of Janeway et al Immunobiology, Third Edition, 1997.

EP 0 759 466 teaches as above, and also teaches that compositions of antibodies to the human IL-12 beta2 receptor proteins and fragments thereof, can be used in combination with other antagonists to treat autoimmune diseases (see entire patent especially page 8, lines 9-16.

However '466 does not specifically teach a composition comprising a monoclonal antibody to a costimulatory molecule and a monoclonal antibody to the IL-12 beta2 receptor recited by instant claims 14 and 18.

Janeway teaches that in a variety of autoimmune diseases, self antigens are presented to TH1 cells (see page 12:17). Janeway teaches on page 9:30 that CD4 T cells initially stimulated by IL12 develop into TH1 cells, and on page 7:25 that Th1 cells mediate their effects through co-stimulatory molecules.

Therefore one who wanted to treat autoimmune diseases would be motivated to administer to a patient suffering from an autoimmune disease a composition which would interfere with the Th1 immune mediators of autoimmune diseases, comprising a monoclonal

antibody to the human IL-12 beta2 receptor proteins and fragments as taught by '466 and an antagonists against costimulatory molecules such as CD40 as taught by Janeway et al. because interfering with costimulatory molecules and IL-12 beta2 receptor function would decrease the autoimmune symptoms mediated by autoimmune TH1 cells.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Response to Arguments

Applicant traverses the rejection on the grounds that the primary reference, as discussed above, does not disclose antibodies that "prevent dimerization of the IL-12R beta 2 chain mediated phosphorylation of STAT4 or dimerization of the IL-12R beta 1 chain , as required by the claims. However, as discussed above, said recited functional limitations are inherent properties of the referenced antibodies blocking the binding of IL-12 to said IL-12R, for the reasons discussed supra.

Allowable Subject Matter

Claims 11-12 and 17 are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy M. DeCloux whose telephone number is 703 306-5821. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 703 308-3973. The fax phone numbers for the

organization where this application or proceeding is assigned are 703 872-9306 for regular communications and 703 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-0196.

Amy DeCloux, Ph.D.
Patent Examiner,
April 17, 2003

Patrick J. Nolan, Ph.D.
Primary Patent Examiner,
Group 1640